Test Material: CGA 359009 (transformation product of Pymetrozine)

MRID: 49921302

Title: ^{14}C-CGA359009 (Metabolite of Pymetrozine). ^{14}C-CGA359009 – Degradation in One Soil Incubated Under Aerobic Conditions. Final Report.
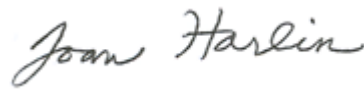
EPA PC Code: 101103 (for pymetrozine)

OCSPP Guideline: 835.4100

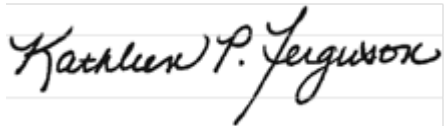**For CDM/CSS-Dynamac JV**

Primary Reviewer: Joan Harlin   **Signature:**

Date: 11/10/16

Secondary Reviewer: Kathleen Ferguson   **Signature:**

Date: 11/10/16

Quality Assurance Manager: Joan Gaidos   **Signature:**

Date: 11/10/16

This Data Evaluation Record may have been altered by the Environmental Fate and Effects Division subsequent to signing by CDM/CSS-Dynamac JV personnel.

Aerobic degradation of CGA 359009, a transformation product of pymetrozine, in one soil

Report: MRID 49921302. Völkl, S. 2013. ^{14}C-CGA359009 (Metabolite of Pymetrozine). ^{14}C-CGA359009 – Degradation in One Soil Incubated Under Aerobic Conditions. Final Report. Unpublished study performed by RCC Ltd, Environmental Chemistry & Pharmanalytics, Itingen, Switzerland; sponsored by Syngenta Crop Protection AG, Basel, Switzerland; and submitted by Syngenta Crop Protection, LLC, Greensboro, North Carolina. Report No.: 848395. Task No.: TK0290227. Experiment started June 20, 2003, and completed October 28, 2003 (p. 12). Final report issued April 16, 2004.

Document No.:   MRID 49921302

Guideline: OCSPP 835.4100

Statements: The study was conducted according to OECD and Swiss GLP standards (p. 6). Signed and dated Data Confidentiality, GLP, and Quality Assurance statements were provided (pp. 2-3, 5-8). A certification of the authenticity of the report was not included; an audit of the final report is listed in the Quality Assurance statement (p. 8).

Classification: This study is SUPPLEMENTAL. A major transformation product, comprising >10% of the applied radioactivity (12.7% of the applied at day 7) was not identified. Sampling intervals were too infrequent to accurately calculate the rate of dissipation of CGA 359009; *ca*. 70% of the applied had dissipated by the second sampling interval (3 days posttreatment).

PC Code: 101103 (for pymetrozine)

Reviewer: Jessica Joyce, MS, Fate Scientist   Signature:
                 U.S. EPA   Date: July 19, 2017

Secondary   Rochelle F. H. Bohaty, PhD, Senior Chemist   Signature:
Reviewer: U.S. EPA   Date: July 19, 2017

EXECUTIVE SUMMARY

The aerobic transformation of [pyridinyl-5-^{14}C] CGA 359009, a transformation product of pymetrozine, was studied in a sandy clay loam soil ("18 Acres"; pH 6.0 in KCl) from the UK that was incubated in darkness at $20 \pm 2°C$ and a soil moisture content of 40% of its maximum water holding capacity for 100 days. The soil was treated at 0.1 mg a.i./kg, equivalent to a field application rate of 0.089 lb a.i./A (assuming 1 g/cm^3 dry bulk density of soil, and a thickness of 10 cm in field soil). Duplicate samples (two entire flasks) of each treatment were collected at each sampling interval. It was not confirmed that aerobic conditions were maintained in the soils throughout the study. The soil was viable at study initiation and termination.

Overall mass balances averaged $96.8 \pm 1.6\%$ of the applied (range 93.6-99.2%). There was no clear pattern of loss of residues over time.

Observed DT$_{50}$ values, calculated half-lives, and information on transformation products are listed in **Table 1**. CGA 359009 dissipated with a t$_{R \ IORE}$ value (IORE) of 2.55 days. One major transformation product was identified.

Total extractable radioactivity declined from 95.1% of the applied at time 0 to 11.6% at 100 days, posttreatment. Unextracted radioactivity increased to a maximum of 48.1% of the applied at 56 days and was 45.0% at 100 days. At study termination, CO_2 totaled maximum of 42.7% of the applied. Organic volatiles were <0.1% of the applied throughout the study.

Table 1. Results Synopsis: Aerobic Soil Metabolism of CGA 359009.

Soil Location and Texture (Temperature, pH)	Observed DT_{50} (days)	Calculated Half-life (days)[1]	Model Parameters and Statistics	Transformation Products (maximum % AR, associated interval)[2]	
				Major	**Minor**
UK Sandy clay loam soil (20°C, pH 6.0)	<3 days	$t_{R\ IORE} =$ 2.55 IORE	$C_0 = 91.3$ $N = 1.64$ $k = 0.0343$	M4 (15.6%, 7 days) Unextracted residues (48.1%, 56 days) CO_2 (42.7%, 100 days)	None

1 Calculated half-lives and model parameters in accordance with NAFTA kinetics guidance (USEPA, 2012);
   Indeterminate Order Rate Equation (IORE).
2 AR means "applied radioactivity".
M4 = CGA 300407; Pyridine-3-carbaldehyde.

I. Materials And Methods

A. Materials:

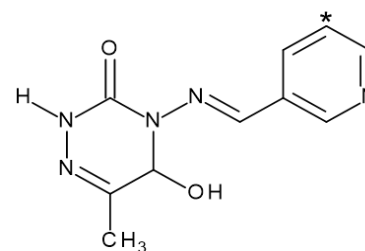**1. Test Material**   [Pyridinyl-5-^{14}C]-labeled CGA 359009 (p. 16)

   Specific activity: 1.44 MBq/mg (p. 16)

   Radiochemical purity: 100.0%

   Chemical purity: Not reported

   Batch No.:   ILA-329.1

Solubility in water: Not reported

2. Reference Compounds: The following standards were used in the analysis (**Table 2**).

Table 2. Reference Compounds.

Applicant's Code Name	Chemical Name	Purity (%)	Batch/Lot No.
CGA 359009	5-Hydroxy-6-methyl-4-[(pyridin-3-ylmethylene)-amino]4,5-dihydro-2H-[1,2,4]triazin-3-one	99.0	DAH-XXI-96-2
CGA 180777	Nicotinic acid	100.0	72309/2
CGA 300407	Pyridine-3-carbaldehyde	92.0	RV-2371
CGA 363431	5-Hydroxy-6-methyl-4-[(6-oxo-1,6-dihydro-pyridin-3-ylmethylene)-amino]-4,5-dihydro-2H-[1,2,4]triazin-3-one	95.0	MLA-224/2

Data obtained from p. 15 and Table 1, 29 of the study report.

3. Soil: Soil collection and characterization are summarized in **Table 3** and **Table 4**, respectively.

Table 3. Description of Soil Collection and Storage.

Description	Details
Geographic location	Winkfield, Berkshire, UK
Site Description	Grass-covered field
Soil series	Not reported. Identified as "18 Acres".
Pesticide use history at the collection site	None for at least 5 years
Collection date	May 27, 2003
Collection procedures	In reference to ISO 10381-6
Sampling depth	5-10 cm
Storage conditions	In reference to ISO 10381-6
Storage length	Immediately after arrival, and before treatment, the soil was taken for acclimation to room temperature for 6 days.
Soil preparation	Vegetation, larger soil fauna, and stones were removed and the soil was sieved (2 mm). The soil was acclimated at room temperature for 6 days prior to use in the study. The soil was finger crumbled and turned over frequently to avoid excessive surface drying, and watered as needed.

Data obtained from p. 17 of the study report.

Table 4. Properties of the Soils.

Property	Details
Soil Texture (USDA)	Sandy clay loam
% Sand	49.2
% Silt	27.5
% Clay	23.3
pH in KCl	6.0
Organic carbon (%)	2.7
Organic matter (%)[1]	4.6
Cation Exchange Capacity (meq/100 g) (method not reported)	20.7
Soil Moisture Content (%)	
pF 1.0 (MWC)	68.9
40% MWC	27.6
pF 2.0	33.0
pF 2.5	26.3
Bulk density (disturbed, g/cm^3)	Not reported
Microbial Biomass (mg C/kg soil)	
At about start of incubation	42.1
At Day 101 of incubation	42.5
Soil taxonomic classification	Not reported

Data obtained from Table 2, p. 30 of the study report. The soil texture was confirmed using USDA-NRCS technical support tools.

1 Calculated by the reviewer using the equation: organic matter (%) = organic carbon (%) x 1.724.

B. STUDY DESIGN

1. Experimental Conditions: (Summarized in **Table 5**).

Table 5. Experimental Design

Property	Details
Duration of the test (days)	100 days
Soil condition (Air dried/fresh)	Fresh
Soil (g/replicate)	100 g (dry wt)
Application rates	
Nominal	0.1 mg a.i./kg dry wt of soil
Actual	Not reported
Control conditions (if used)	Sterile controls were not used.
Number of Replicates	
Controls (if used)	Sterile controls were not used.
Treatment	Two flasks from each treatment were collected at each sampling interval.
Test apparatus	
Type/material/volume	The test system consisted of *ca*. 1-L glass flasks (*ca*. 10.6 i.d.) containing moist treated soil (100 g dry wt) were attached to flow-through volatile trapping systems, continuously ventilated with humidified air, and incubated in an air-conditioned room maintained at $20 \pm 2°C$. A minimal volumetric flow rate (not reported) was used to keep soil water losses to a minimum. The test system is illustrated in Figure 1, p. 35.
Details of traps for CO_2 and other volatiles (if any)	Humidified air was ventilated through a sample flask, then through one tube of 2N NaOH and one tube of ethylene glycol. The volatile trapping system is illustrated in Figure 1, p. 35.
If no traps were used, is the system closed/open?	Volatile traps were used.
Identity and concentration of co-solvent	Acetone
Test Material:	
Volume of the test solution used/treatment	0.250 mL/100 g
Application method	The test solution was applied to the soil surface using a Hamilton syringe.
Is the co-solvent evaporated?	Yes
Any indication of the test material adsorbing to the walls of the test apparatus?	None
Experimental conditions:	
Temperature (°C)	$20 \pm 2°C$.
Continuous darkness	Yes
Moisture content	40% of maximum water holding capacity
Moisture maintenance method	Water loss was compensated for by weighing the samples weekly until Day 23 and thereafter for *ca*. 14 days. The evaporated water was added followed by mixing, as necessary.
Other details (if any)	None

Data obtained from pp. 17-19 and Figure 1, p. 35, of the study report.

2. Sampling During Study Period: (Details summarized in **Table 6**).

Table 6. Sampling During Study Period

Criteria	Details
Sampling intervals (days)	0, 3, 7, 10, 14, 28, 56, and 100 days.
Sampling method	Duplicate flasks of each treatment were collected at each sampling interval.
Method of collection of CO_2 and organic volatile compounds	Volatile trapping solutions were exchanged at the sampling dates or in about 14-day intervals.
Sampling intervals/times for:	
Sterility check (if used)	Sterile controls were not used.
Moisture content	Water loss was compensated for by weighing the samples weekly until Day 23 and thereafter for *ca*. 14 days. The evaporated water was added followed by mixing, as necessary.
Redox potential, other	Redox potential was not measured.
Sample storage before analysis	Sample storage was not described. It was not reported whether the soils were stored prior to extraction or the soil extracts were stored prior to analysis.
Other observation (if any)	None.

Data obtained from pp. 18-19 of the study report.

3. Analytical Procedures:

Extraction Methods: Soil samples (entire vessel) were extracted up to five times with acetonitrile:water (4:1, v:v) by shaking for *ca*. 30 minutes at room temperature, then centrifuged for 5-10 minutes (2000 rpm; p. 19). The samples were then Soxhlet extracted with acetonitrile:water (4:1, v:v) for 4 hours (p. 20). Individual extracts were analyzed for radioactivity using LSC. Thereafter, all extracts were combined and analyzed using LSC. For further analysis by TLC and/or HPLC, combined extracts from Day 0, 3, 7, and 100 samples were concentrated by rotary evaporation under reduced pressure (*ca*. 30°C) and re-analyzed using LSC.

For Day 3 and 7 samples, a part of the radioactivity evaporated with the solvent during concentration of the organic extracts, but was recovered in the acetonitrile:water distillate collected during concentration (p. 20). The remaining aqueous phase was analyzed separately using LSC. The extracts obtained from Day 10, 14, 28, and 56 samples were concentrated until the organic solvent evaporated. The remaining aqueous phase was partitioned with ethyl acetate up to three times. The aqueous phase and combined ethyl acetate extracts after partitioning were analyzed using LSC. The aqueous phase and organic extracts were concentrated under reduced pressure as described, and analyzed using TLC.

Determination of Unextracted Residues: The extracted soils were air-dried and homogenized, and aliquots were analyzed for total remaining radioactivity using LSC following combustion (p. 20).

Determination of Volatile Compounds: Aliquots of the trapping solutions were analyzed by LSC (p. 19). The presence of CO_2 in the trapping solutions was confirmed by precipitation with barium chloride.

Total radioactivity measurement: Total [^{14}C]residues were determined by summing the concentrations of residues in the soil extracts, extracted soil, and volatile traps (Table 3, p. 31).

Derivatization method: A derivatization method was not employed.

Identification and quantification of Parent and Transformation Compounds: Aliquots of the extracts were analyzed by one-dimensional TLC on silica gel plates developed in dichloromethane:methanol:acetic acid (9:1,1, v:v:v); ethyl acetate:ethanol:ammonia (25%):water (65:23:4:12, v:v:v:v); and chloroform:methanol:water (60:30:5, v:v:v); and chloroform:methanol:water (60:30:5), and by two-dimensional TLC on silica gel plates developed in dichloromethanoe:methanol:acetic acid (9:1:1, v:v:v) in the first direction and ethyl acetate:ethanol:ammonia (25%):water (65:23:4:12, v:v:v:v) in the second direction (p. 21). [^{14}C]compounds were identified by comparison to reference standards that were cochromatographed with the samples and visualized under UV light (p. 22). Radioactive regions were located and quantified with a phosphor imager or liner analyzer.

To confirm the results of TLC analysis, aliquots of the soil extracts were analyzed by HPLC using a Nucleosil 100-5 C18 or Nucleosil 120 C18 column eluted with a gradient mobile phase of (A) water and (B) acetonitrile or methanol, with UV and radioactive flow detection (pp. 22-23). HPLC peaks were identified by comparison to reference standards that were cochromatographed with the samples (p. 27).

Detection Limits (LOD, LOQ) for the Parent and Transformation Products: Limits of Detection (LOD) and Quantification (LOQ) were set at 2x and 3x background, respectively (Appendix B, pp. 58, 60).

For LSC, the LODs were 2.1222% of the applied for extractable residues, 0.4699% for combustion, and 0.4554% for CO_2 (Appendix B, p. 58). The respective LOQs were 3.18%, 0.7049%, and 0.6831% of the applied.

For TLC, the LODs for [^{14}C]compounds were 0.479-1.725% of the applied and the LOQs were 0.718-2.587% of the applied (Appendix B, p. 61).

For HPLC, LODs and LOQs were not reported.

II. Results and Discussion

A. Data

Study results including total mass balances and distribution of radioactivity are presented in **Tables 7a-7b**. No determinations were made to verify that aerobic conditions were maintained in the soils. The soil was viable at study initiation and termination (p. 26; Table 2, p. 30).

B. Mass Balance

Overall mass balance averaged 96.8 ± 1.6% of the applied (range 93.6-99.2%; Table 3, p. 31). There was no clear pattern of loss of residues over time.

C. Unextracted and Extractable Residues

Total extractable radioactivity declined from 95.1% of the applied at time 0 to 11.6% at 100 days posttreatment (Table 3, p. 31). Unextracted radioactivity increased to a maximum of 48.1% of the applied at 56 days and was 45.0% at 100 days.

D. Volatilization

At study termination, CO_2 totaled maximum of 42.7% of the applied (Table 3, p. 31). Organic volatiles were <0.1% of the applied throughout the study.

Table 7. Aerobic transformation of [5-pyridinyl-^{14}C]CGA 359009, expressed as a percentage of the applied radioactivity, in sandy clay loam soil.

Sampling Interval (days)	0		3		7		10		14		28		56		100	
Replicate Number	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B
CGA 359009 (M1)	90.7	91.8	28.7	27.4	7.1	5.5	11.5	8.5	7.3	6.4	2.0	2.3	0.8	0.7	0.3	0.3
M2	n.d.	n.d.	3.2	2.4	5.0	4.1	4.7	5.0	5.3	5.3	5.6	5.2	5.2	5.9	4.4	5.3
M3	n.d.	1.0	5.5	6.1	11.2	12.7	7.4	8.4	4.6	5.7	3.0	2.8	1.5	1.4	0.7	0.7
M4	3.6	2.2	10.1	13.1	13.8	15.6	3.6	5.5	2.8	3.6	0.2	1.2	1.1	0.7	n.d.	n.d.
M11	n.d.	n.d.	7.5	4.8	1.2	0.9	1.2	1.1	0.7	0.6	n.d.	0.2	0.3	0.3	n.d.	n.d.
Sum of radioactive fractions[1]	0.4	n.d.	12.0	10.0	10.2	7.4	9.9	13.1	11.6	10.6	8.5	7.4	4.1	4.5	4.7	5.3
Extracted residues	94.8	95.1	55.6	53.0	33.1	32.7	23.3	26.5	19.8	19.2	8.7	9.0	2.6	2.6	1.5	2.2
Soxhlet extracted residues	n.p.	n.p.	11.4	10.7	15.4	13.5	15.0	15.0	12.4	13.1	10.6	10.1	10.4	10.9	8.6	9.4
Total extracted residues	94.8	95.1	67.0	63.7	48.5	46.2	38.3	41.5	32.2	32.3	19.3	19.1	13.0	13.5	10.1	11.6
Unextracted residues	3.9	3.5	23.9	24.0	33.7	35.5	38.1	36.8	41.5	41.8	47.0	44.0	48.1	46.8	44.9	45.0
CO_2	n.p.	n.p.	7.7	8.3	15.0	14.7	18.2	19.0	22.6	22.9	30.8	31.0	35.8	36.2	38.5	42.7
Organic volatiles	n.p.	n.p.	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
Mass balance	98.7	98.6	98.6	96.0	97.3	96.4	94.6	97.2	96.4	97.0	97.2	94.1	97.0	96.5	93.6	99.2

Data obtained from Table 3, p. 31 and Table 5, p. 33 of the study report.
[1]Comprised of M5, M6, M7, M8, M9, M10, M12, M13, and M14, none exceeding 4.2% of the applied radioactivity.
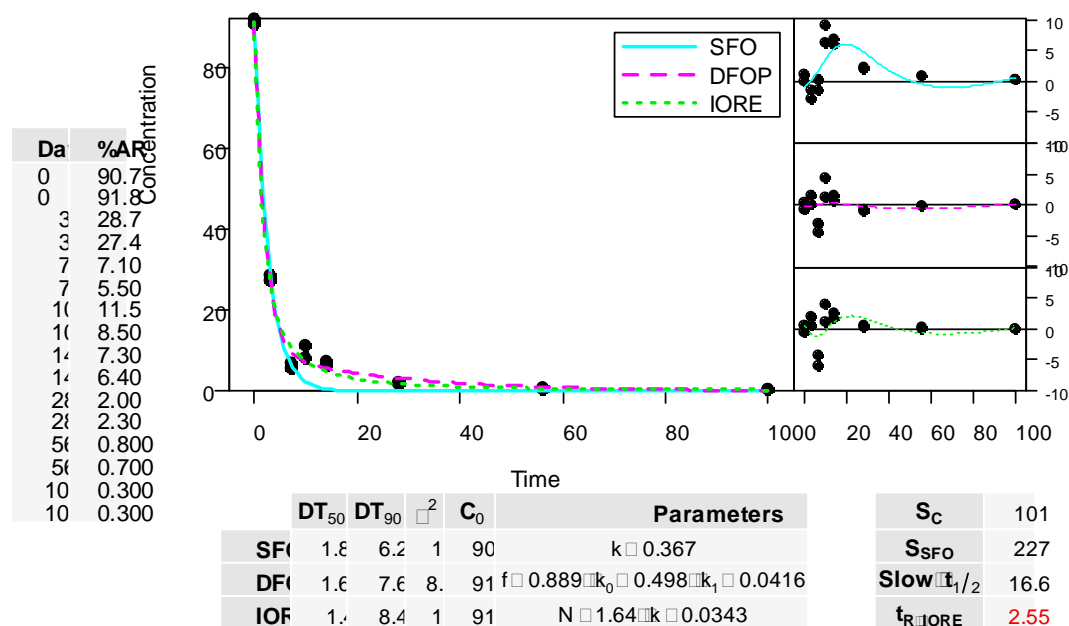 n.d. = not detected; n.p. = not performed.
M4 = CGA 300407; Pyridine-3-carbaldehyde.

E. Transformation of the Test Compound: Transformation kinetics of the parent compound in the total system are summarized in the following **Figure**. Transformation product information is summarized in **Table 8**.

Using first order kinetics (Modelmaker, v. 3.0.2), the study author determined a DT50 value for CGA 359009 of 1.9 days in the sandy clay loam soil (p. 28; Table 6, p. 34). Reviewer calculated half-live values is 2.6 days.

Aerobic metabolism of CGA 359009 in sandy clay loam soil

Da	%AR
0	90.7
0	91.8
3	28.7
3	27.4
7	7.10
7	5.50
10	11.5
10	8.50
14	7.30
14	6.40
28	2.00
28	2.30
56	0.800
56	0.700
10	0.300
10	0.300

Kinetics models: Single First Order (SFO); Double First Order in Parallel (DFOP), and Indeterminate Order Rate Equation (IORE). Calculated half-lives and model parameters in accordance with the NAFTA kinetics guidance (USEPA, 2012).

	DT_{50}	DT_{90}	^{2}	C_0	Parameters		
SFO	1.8	6.2	1	90	$k = 0.367$	S_C	101
DFO	1.6	7.6	8.	91	$f = 0.889$, $k_0 = 0.498$, $k_1 = 0.0416$	S_{SFO}	227
IOR	1.4	8.4	1	91	$N = 1.64$, $k = 0.0343$	Slow $t_{1/2}$	16.6
						t_{R-IORE}	2.55

Observed nonvolatile transformation products are described in **Table 8**. One transformation product was identified.

Table 8. Transformation Products of CGA 359009 in Soil.

	Transformation Products	Maximum %AR Observed	Associated Interval (days)	Final %AR Observed	Final Interval (days)
UK Sandy clay loam (20°C, pH 6.0)	CGA 300407 (M4)	15.6	7	n.d.	100

Data obtained from Table 5, p. 33 of the study report.

An aerobic transformation pathway for CGA 359009 in soil was not provided by the study author.

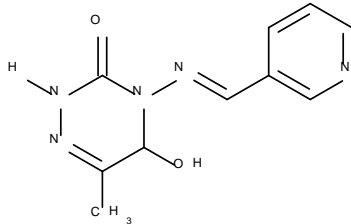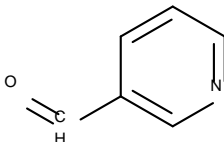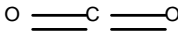### III. STUDY DEFICIENCIES AND REVIEWER'S COMMENTS

1. Significant levels (48.1% of the applied) of unextracted residues were detected (Table 3, p. 31). The study author failed to use solvents with a range of dielectric constants (including a nonpolar solvent) to maximize extraction of the residues.
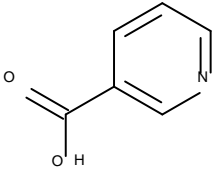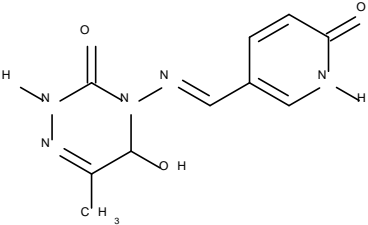
2. Sampling intervals were too infrequent to accurately calculate the rate of dissipation of CGA 359009; *ca*. 70% of the applied had dissipated by the second sampling interval (3 days posttreatment (Table 5, p. 33).

3. One major transformation product, M3, comprising >10% of the applied radioactivity (12.7% of the applied at day 7) was not identified (Table 5, p. 33).

4. Handling of the soil extracts, extracted soil, and trapping solutions prior to analysis was not reported. It was not stated if the soil was stored prior to extraction. Length and conditions of storage of the soil extract prior to analysis were not reported. Storage of samples when not in use was not described.

5. Conditions of storage of the soil prior to use in the study were not reported, however the radiochemical purity of CGA 359009 prior to treatment was determined to be 99.5%, and post-treatment had a purity of 98.9%.

6. The soil was from the UK, and was not compared to soils from the US.

7. It was not confirmed that aerobic conditions were maintained in the soils throughout the study.

IV. REFERENCES

1. U.S. Environmental Protection Agency. 2008. Fate, Transport and Transformation Test Guidelines, OCSPP 835.4100, Aerobic Soil Metabolism. Office of Chemical Safety and Pollution Prevention, Washington, DC. EPA 712-C-08-016.

2. U.S. Environmental Protection Agency. 2012. NAFTA Guidance for Evaluating and Calculating Degradation Kinetics in Environmental Media.

DER ATTACHMENT 1. CGA 359009 and Its Environmental Transformation Products. [A]

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum %AR (day)		Final %AR (study length)
		PARENT					
CGA 359009 (CSAA441607)	**IUPAC:** 4,5-Dihydro-5-hydroxy-6-methyl-4-[(3-pyridinylmethylene)amino]-1,2,4-triazine-3-(2H)-one **Formula:** $C_{10}H_{11}N_5O_2$ **MW:** 233.2 g/mol **SMILES:** CC1=NNC(=O)N(\N=C\c2cccnc2)C1O		835.4100 Aerobic soil metabolism	49921302	PRT		PRT
		MAJOR (>10%) TRANSFORMATION PRODUCTS					
CGA 300407 (M4)	**IUPAC:** 3-Pyridinecarboxaldehyde **Formula:** C_6H_5NO **MW:** 107.1 g/mol **SMILES:** O=Cc1cccnc1		835.4100 Aerobic soil metabolism	49921302	Sandy clay loam	**15.6%** (7 d)	ND (100 d)
Carbon dioxide	**IUPAC:** Carbon dioxide **Formula:** CO_2 **MW:** 44 g/mol **SMILES:** C(=O)=O		835.4100 Aerobic soil metabolism	49921302	Sandy clay loam	**42.7%** (100 d)	**42.7%** (100 d)
Unextractable residues	NA	NA	835.4100 Aerobic soil metabolism	49921302	Sandy clay loam	**48.1%** (56 d)	**45.0%** (100 d)

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum %AR (day)	Final %AR (study length)
**MINOR (<10%) TRANSFORMATION PRODUCTS**					
No minor transformation products were identified.					
**REFERENCE COMPOUNDS NOT IDENTIFIED**					
CGA 180777	**IUPAC:** Nicotinic acid **Formula:** $C_6H_5NO_2$ **MW:** 123.1 g/mol **SMILES:** OC(=O)c1cccnc1		835.4100 Aerobic soil metabolism	49921302	NA	NA
CGA 363431	**IUPAC:** 5-Hydroxy-6-methyl-4-[(6-oxo-l,6-dihydro-pyridine-3-ylmethylene)-amino]-4,5-dihydro-2H-[l,2,4]triazine-3-one **Formula:** $C_{10}H_{11}N_5O_3$ **MW:** 249.2 g/mol **SMILES:** CC1=NNC(=O)N(\N=C\C2=CNC(=O)C=C2)C1O		835.4100 Aerobic soil metabolism	49921302	NA	NA

[A] AR means "applied radioactivity". MW means "molecular weight". PRT means "parent". ND means "not detected". NA means "not applicable".

DER Attachment 2. Statistics Spreadsheets and Graphs

DER Attachment 3: Calculations

Calculations were performed by the reviewer using PestDF, and the following equations.

Single First-Order (SFO) Model

$$C_t = C_0 e^{-kt}$$
(eq. 1)

where,

C_t = concentration at time t (%)
C_0 = initial concentration (%)
e = Euler's number (-)
k = SFO rate constant of decline (d^{-1})
t = time (d)

The SFO equation is solved with PestDF by adjusting C_0 and k to minimize the objective function (S_{SFO}) shown in equation 9.

$$DT_{50} = \text{natural log (2)}/k$$
(eq. 2)

$$DT_{90} = \ln (10)/k$$
(eq. 3)

Indeterminate Order Rate Equation (IORE) Model

$$C_t = \left[C_0^{(1-N)} - (1-N) k_{IORE} t \right]^{\left(\frac{1}{1-N}\right)}$$
(eq. 4)

where,

N = order of decline rate (-)
k_{IORE} = IORE rate constant of decline (d^{-1})

This equation is solved with PestDF by adjusting C_0, k_{IORE}, and N to minimize the objective function for IORE (S_{IORE}) (See equation 9). Half-lives for the IORE model are calculated using equation 5, which represents a first-order half-life that passes through the DT_{90} of the IORE model. (Traditional DT_{50} and DT_{90} values for the IORE model can be calculated using equations 6 and 7.)

$$t_{IORE} = \frac{\log(2)}{\log(10)} \frac{C_0^{1-N}\left(1-0.1^{(1-N)}\right)}{(1-N)k_{IORE}}$$
(eq. 5)

$$DT_{50} = \frac{(C_0/2)^{(1-N)} - C_0^{(1-N)}}{k(N-1)}$$
(eq. 6)

$$DT_{90} = \frac{(C_0/10)^{(1-N)} - C_0^{(1-N)}}{k(N-1)}$$
(eq. 7)

Double First-Order in Parallel (DFOP) Model

$$C_t = C_0 g^{-k_1 t} + C_0 (1-g)^{-k_2 t}$$ (eq. 8)

where,

g = the fraction of C_0 applied to compartment 1 (-)
k_1 = rate constant for compartment 1 (d^{-1})
k_2 = rate constant for compartment 2 (d^{-1})

If $C_0 \times g$ is set equal to a and $C_0(1-g)$ is set equal to c, then the equation can be solved with R kinetics software for a, c, k_1, and k_2 by minimizing the objective function (S_{DFOP}) as described in equation 9.

DT_{50} and DT_{90} values can be calculated using equations 2 and 3, with k_1 or k_2 in place of k.

Objective Function: SFO, IORE, and DFOP are solved by minimizing the objective function (S_{SFO}, S_{IORE}, or S_{DFOP}).

$$S_{SFO}, S_{IORE}, \text{ or } S_{DFOP} = \Sigma (C_{model, t} - C_{d,t})^2$$ (eq. 9)

where,

S_{SFO} , S_{IORE}, or S_{DFOP} = objective function of kinetics model fit ($\%^2$)
n = number of data points (-)
$C_{model,t}$ = modeled value at time corresponding to $C_{d,t}$ (%)
$C_{d,t}$ = experimental concentration at time t (%)

Critical Value to Determine Whether SFO is an Adequate Kinetics Model

If S_{SFO} is less than S_C, the SFO model is adequate to describe kinetics. If not, the faster of t_{IORE} or the DFOP DT_{50} for compartment 2 should be used.

$$S_c = S_{IORE} \left(1 + \frac{p}{n-p} F(\alpha, p, n-p) \right)$$ (eq. 10)

where,

S_c = the critical value that defines the confidence contours ($\%^2$)
p = number of parameters (3 in this case)
α = the confidence level (0.50 in this case)
$F(\alpha, p, n-p)$ = F distribution with α level of confidence and degrees of freedom p and n-p